

Executive Summary

INTRODUCTION

In early 2009, a number of incidents concerning pharmaceutical products in Hong Kong had caused public concerns on drug safety. The Food and Health Bureau (FHB) and Department of Health (DH) took immediate measures to address the concerns, including the inspection of all local drug manufacturers. As a longer term measure, it was decided that a comprehensive review on the existing regime for the regulation of pharmaceutical products (western medicines) be conducted.

SETTING UP OF THE REVIEW COMMITTEE ON THE REGULATION OF PHARMACEUTICAL PRODUCTS IN HONG KONG

2. The Review Committee on the Regulation of Pharmaceutical Products in Hong Kong (Review Committee) chaired by the Permanent Secretary for Health with members from the pharmaceutical sector, medical profession, academia, patient groups and consumer representative was set up on 24 March 2009. In consideration of the wide range and complexity of the issues to be examined, the Review Committee set up two Sub Committees, one on drug manufacturing and another on drug distribution and procurement to examine the various issues in depth. A Task Force was also set up under the chairmanship of the Director of Health to provide expert advice to the Review Committee, and an Expert Group was set up to give advice on the microbiological hazards on drug manufacturing. The background of the review, the terms of reference, membership and work of the Review Committee, the two Sub Committees, the Task Force and the Expert Group are set out in Chapter 1 (and Annexes A to C) of this report.

PRESENT SITUATION

3. The current drug regulatory regime adopts a risk management, dual target and multi-pronged approach backed by the law. The dual targets are the pharmaceutical products and the pharmaceutical trade. Multi-pronged approach embraces legal requirements and administrative measures which provide the framework of the control system, education for the pharmaceutical sector to equip them with the necessary professional knowledge, promotion and publicity to remind the public of the importance of drug safety, and a penalty system to deter the pharmaceutical sector from malpractices. The control system starts at

the source of supply of drugs and follow through each point in the production line and the supply chain until the drug reaches its target patients. The framework of the regime is similar to those of many overseas jurisdictions, but the implementation details could differ from one place to another. Chapter 2 of the review report provides an overview of the existing regulatory regime.

UNDERLYING PRINCIPLES OF THE REGULATORY REGIME

4. The Review Committee agrees that the regulatory regime of the pharmaceutical sector should adhere to the following key principles and objectives:

- (a) protecting public health and ensuring patient safety is the top priority;
- (b) the regulatory regime should be able to maintain public confidence on the usage of drugs;
- (c) the regulatory regime should be able to sustain and improve the standard of the pharmaceutical sector, but at the same time able to identify and address any bad practices;
- (d) the regulatory regime should be fair, accountable, consistent and transparent; and
- (e) the regulatory regime has to strike a fine balance between effective regulation and the challenges to the trade and the professionals.

5. The Review Committee agrees that while the Government has the responsibility to regulate, the pharmaceutical trade has the responsibility to comply with the prescribed requirements and standards, to enhance governance and the audit process. The pharmacist profession and all healthcare professionals have the responsibility to discharge their duties and uphold their high professional standards.

FINDINGS AND RECOMMENDATIONS OF THE REVIEW

6. With the above principles in mind, the Review Committee has examined in detail the existing regulatory regime. It considers that the framework and the rationale behind the existing regime is sound and while it should continue to be adopted, the coverage and depth of the regulatory

measures should be enhanced. The Review Committee is, however, mindful of the implementation details and considers that while changes should be made to enhance the effectiveness of the regime, various proposed new measures should have an implementation programme, taking into account the lead time required to acquire resources, train the personnel both within DH and in the trade, set up the system for the stakeholders to follow or adapt, and to take forward the legislative amendments. Nevertheless, proposals which are key to enhance drug safety should be implemented with priority. At the same time, the Review Committee believes that the pharmaceutical sector plays a pivotal role in protecting the integrity of the system by observing self-discipline and upholding the pharmacist professional standards.

7. The Review Committee has made a total of 75 recommendations, covering the following different aspects as summarised in the ensuing paragraphs (and Annexes D and E).

(a) Regulation of drug manufacturers and Good Manufacturing Practices (GMP) Scheme (Chapter 3)

- (i) **To upgrade the current Hong Kong GMP standard to a higher international standard:** GMP is a quality assurance approach used by the drug manufacturing industry worldwide to ensure that products are consistently produced and controlled throughout the manufacturing process. The spirit of GMP emphasizes that the assessment of good quality should be based on scrutiny of the manufacturing processes and not by testing of the end product alone. Hong Kong is now adopting the GMP standard promulgated by the World Health Organization (WHO) in 1995. The Review Committee recommends that in about two years' time the GMP standard of Hong Kong be first upgraded to the standard promulgated by WHO in 2007, and in about another two years' time it should be upgraded to an even higher standard devised by the Pharmaceutical Inspection Cooperation Scheme, i.e. the PIC/S standard. The PIC/S standard includes a stricter control over the use of active pharmaceutical ingredients for drug manufacturing, more stringent qualification requirements for the position of the authorized person who oversees the entire drug manufacturing process, a more enhanced inspection and licensing arrangement, and a more comprehensive training framework for all levels of personnel involved in the GMP system. This recommendation should be implemented with priority.

- (ii) **To introduce microbiological monitoring for non-sterile drugs during the manufacturing process:** In the light of the earlier incident of fungal contamination of drugs, the Review Committee recommends that local manufacturers be required to conduct microbiological tests for non sterile drugs. Drug manufacturers will be required to adopt a new model for microbiological monitoring, including the carrying out of microbiological tests on raw materials, limiting the time whereby the granules can be kept to not more than 48 hours, conducting microbiological tests on finished products and including microbiological testing in the stability studies of all products. If a manufacturer intends to adopt a longer holding time, he must provide the necessary data and evidence supporting the proposed holding time to DH for consideration. This recommendation should be implemented with priority.
 - (iii) **To tighten up the qualification of the Authorized Person (AP) by increasing the required number of years of industrial experience and imposing requirements on training:** A formal set of criteria regarding the qualifications of the AP will be set, alongside with the introduction of a structured training programme and a mechanism to ensure that APs will take responsibility for the quality, safety and efficacy of their drug products. In the meantime, the position of AP will still be required to be filled by pharmacist with relevant experience. In the long run when a licensing or listing system for APs and additional formal certified GMP training have been developed, consideration will be given to allowing additionally non-pharmacists with the required experience and training to assume the position of AP.
 - (iv) **To require all companies which undertake repackaging activities, including secondary repackaging in addition to primary repackaging, to have a manufacturing licence:** A new category of repackaging licence will be introduced for such purpose. This recommendation should be implemented with priority.
- (b) **Pre-market control of drugs (Chapter 4)**
- (i) **To require bioavailability and bioequivalence (BABE) studies for drug registration:** BABE refers to the therapeutic equivalence of the same pharmaceutical product manufactured by different manufacturers. BABE studies seek to assess whether a generic

drug produces the same therapeutic effect as the patent drug. This is particularly important for some drugs, such as antiepileptic drugs, where a reduced or excessive therapeutic effect could be harmful to the patient. The Review Committee recommends that BABE studies be required for drug registration. To allow time for the market to build up its capacity for carrying out the studies, the recommendation will be implemented in phases, starting with drugs where a reduced or excessive therapeutic effect could have undesirable consequences.

- (ii) **To Change the term “Poison 毒藥” on drug labels:** The term “poison” in drug labels arouses unnecessary concern of the public regarding the safety of the drug. The Review Committee recommends that alternative terms be devised. One recommendation is to adopt the terms “prescription drugs 處方藥” and “drugs under supervised sale 監售藥”. The Pharmacy and Poisons Board should consult the stakeholders on the most appropriate terms.
 - (iii) **DH to shorten the processing time for drug registration approval:** As a result of manpower constraints, the processing time for approval of registration of drugs, for change of particulars of registered drugs and for clinical trials are quite long. The Review Committee recommends that DH shortens the time by 40% - 50%.
- (c) **Regulation of importers/exporters, wholesalers and retailers (Chapter 5)**
- (i) **To require wholesalers handling non-poisons to apply for a licence:** At present, wholesalers of drugs which are non-poisons (e.g. vitamins) are not subject to licensing control. The Review Committee considers that patients’ health would be affected if these drugs are not handled properly. The Review Committee recommends that DH requires all wholesalers of non-poisons to apply for a licence so that DH could impose licensing requirements on them.
 - (ii) **To require wholesalers to keep transaction records for Part II Poisons and non-poisons:** At present the law only requires wholesaler to keep transaction records for Part I Poisons. The Review Committee recommends that wholesalers also keep transaction records for all pharmaceutical products, including Part II Poisons and non-poisons. This will ensure that drugs are being

procured through a proper channel and the sources can be traced if problems arise.

- (iii) **To introduce a Code of Practice for wholesalers, importers and exporters:** At present there are no guidelines governing the roles and responsibilities of wholesalers, importers and exporters on product quality, as opposed to the GMP compliance for manufacturers. The Review Committee recommends that a Code of Practice be introduced for wholesalers, importers and exporters to follow.
- (iv) **To strengthen the control of the import and export of pharmaceutical products:** The Review Committee recommends DH to deploy a designated team to provide advice to the Customs and Excise Department (C&ED) at ports of entry and to undertake surveillance work.
- (v) **To strengthen the tracking system for drugs imported for re-export purpose:** The Review Committee recommends DH to set up a record and tracking system so that export licence applicants are required to produce the relevant import licences of the imported drugs to be re-exported. This will enable DH staff to keep track of the amount imported and the amount intended to be exported to prevent illegal diversion of drugs imported for re-export purpose into the local market. In the long run, an electronic record system which is inter-operable with C&ED and the Trade and Industry Department should be a more efficient alternative. In addition, the weekly quota of post-shipment consignment checks of licence by C&ED will be increased, taking into account the workload of C&ED staff.
- (vi) **To require retailers handling non-poisons to apply for a licence:** At present, retailers of non-poisons are not required to apply for a licence. Although non-poisons are drugs of lower risk, they will still affect public health if not being handled properly. The Review Committee recommends that retailers selling non-poisons be required to apply for a licence from DH.
- (vii) **To require the presence of pharmacists during all business hours of pharmacies:** At present, a registered pharmacist has to be present in an Authorized Sellers of Poisons (ASPs), i.e. pharmacies, for not less than two-third of its opening hours. The Review Committee recommends that in the long run a registered

pharmacist should be present whenever an ASP is open for business. This will improve the professional services provided by pharmacists. To further enhance the role of pharmacists in the control of the storage and supply of drugs at ASPs, apart from the above proposal, heightened enforcement actions should be taken against non-pharmacists who have violated the law or interfered with the duties of pharmacists. The Review Committee noted that this recommendation should take into account the market operating conditions as well as the availability of sufficient pharmacists and cannot be implemented immediately.

- (viii) **To include in the law the requirement for retailers to follow their Codes of Practice:** The existing Code of Practice for ASPs, i.e. pharmacies, has no legal status for enforcement, and there is no Code of Practice for Listed Seller of Poisons (LSPs), i.e. medicine companies, to follow with regard to the handling of drugs. The Review Committee recommends that a Code of Practice be devised for LSPs and the law be amended to require that both ASPs and LSPs have to follow their respective Codes of Practice.
- (ix) **To empower the Pharmacy and Poisons Board (PPB) to revoke licences of ASPs:** At present the PPB can only stop renewing licences of ASPs at the beginning of each year, but has no authority to revoke the licence during the year. The Review Committee recommends giving such authority to the PPB so that the licence of an ASP can be revoked if it has committed a serious offence.
- (x) **To require retailers and doctors to have written records for drug orders:** This is to ensure that there is proper record and checking mechanism to prevent errors during delivery of drugs which is necessary to protect the safety of patients. The Review Committee notes that the trade would need time to work out a system with the suppliers. In the long run, electronic record should be a more efficient alternative. The Review Committee also notes that the written record requirement is already recommended in the “Good Dispensing Practice Manual” issued by the Hong Kong Medical Association and the Hong Kong Medical Council has advised doctors to observe the Manual. The Hong Kong Doctors Union objects to the mandatory requirement of written order of drugs.

(d) Procurement and supply of pharmaceutical products in the public and private medical sectors (Chapter 6)

- (i) The Hospital Authority (HA) and DH to require suppliers to provide detailed information on the delivery documentation:** HA and DH will require supplier to provide information such as pack size and registration number in the delivery documents to enable more effective checking and verification of drugs received. This recommendation should be implemented with priority.
- (ii) HA and DH to check the quality of drugs:** Microbiological and chemical testings will be conducted to ensure drug quality. This recommendation should be implemented with priority.
- (iii) DH to encourage the private medical sector to follow the proposed set of guiding principles on drug handling:** DH will issue a set of guiding principles for all private hospitals. The principles include the selection, procurement, delivery and receipt, storage and repacking of drugs, staff training and auditing. This recommendation should be implemented with priority.

(e) Post-market control of drugs and Pharmacovigilance (Chapter 7)

- (i) DH to continue the extended coverage for the surveillance of high risk products in the market:** DH has increased the number of drug samples collected in the market for testing to over 2 000 in recent years. The Review Committee recommends DH to continue with such rigorous surveillance and the existing practice of reporting anomalies to the public. This recommendation should be implemented with priority.
- (ii) DH to enhance Pharmacovigilance activities:** Pharmacovigilance is the detection, assessment, understanding and prevention of adverse effects of drugs. DH will promote these activities through education, training and promotion among healthcare professionals and the trade and to foster a culture of awareness of pharmacovigilance.

(f) Risk communication, education and training (Chapter 8)

- (i) DH to set up a dedicated team for education and training:** At present there is no coordination amongst various organizations which provide public education programmes on drug safety. The

Review Committee recommends DH to set up a dedicated team to coordinate the efforts of various parties, to draw up guidelines on risk communication and to perform risk assessment in response to incidents and to recommend risk communication actions. This recommendation should be implemented with priority.

- (ii) **DH to provide more information on drugs to the public:** Drug information in the existing DH's electronic compendium of pharmaceutical products are not comprehensive and user friendly enough. The Review Committee recommends that the content of the compendium be enhanced. The Review Committee also recommends the setting up of a designated website to promote drug safety. This recommendation should be implemented with priority.

(g) Penalty review (Chapter 9)

- (i) **To strengthen the penalty on manufacturers:** The Review Committee recommends authorizing the Manufacturing Licensing Committee of the Pharmacy and Poisons Board to remove the authorized person when he breaches his duties and to stop the production of the manufacturer when the authorized person has been removed.
- (ii) **To require the convicted person to bear the costs for analyzing exhibits in court cases:** The cost for analyzing exhibits in court cases could be substantial. The Review Committee recommends that the law be amended to require the convicted person to bear such costs in order to increase the deterrent effect.
- (iii) **To provide the Court with more background information in prosecution cases:** DH should present more information to the Court to reflect the seriousness of the offence concerned for the Court to consider the penalty proportionate to the seriousness of the offence.

8. Chapter 10 of this report provides a general assessment on the resources implications of implementing the recommendations, while Chapter 11 summarizes the recommendations and concludes the work of the Review Committee. A glossary of terms is at *Annex F* for reference.

WAY FORWARD

9. The Review Committee has completed its task by giving recommendations on the measures to improve the existing regime. The Government will take follow up actions to implement these measures. The Food and Health Bureau will oversee the policy issues, and together with the Department of Health, will take forward the necessary legislative amendments, address the resource implications and requirements involved. The Department of Health and Hospital Authority will also be responsible for the implementation of the recommendations, consulting the stakeholders in the process. The implementation programme of the various recommendations is set out at Annex D. Some of the recommendations will be implemented subject to the passing of the relevant legislative amendments and may require a longer timeframe for implementation. A list of such recommendations is at Annex E.

10. Whilst the recommendations will be implemented in different phases, the Review Committee also recommends that a dedicated office on drugs should be set up to strengthen the regulatory role of the Government in enhancing drug safety in Hong Kong as a matter of priority . The office will plan and direct the implementation of measures relating to drug safety. DH will work closely with the pharmaceutical trade and all stakeholders to plan for the setting up of the office. In the long run, consideration will be given to expanding the office to be a “Centre for Drug Safety”.

11. The Review Committee also notes that the Pharmacy and the Poisons Ordinance needs to be kept under regular review taking into account the changes in the operating environment of the pharmaceutical trade.

12. The Review Committee Chairman expresses her gratitude to all its Members, the pharmaceutical and medical sectors, academia, patient groups and consumer representative for their invaluable advice and unflinching support during the whole course of the review. The recommendations of the Review Committee will be implemented through the tripartite collaboration among the regulatory authority, the trade and consumers. All parties would need to maintain their heightened vigilance against any mal-practices. We believe that the key to the success in raising the standard of the pharmaceutical sector in Hong Kong lies in an effective regulatory regime, the commitment and determination of the professionals to practise to their highest standards and the trade to perform responsibly.

IN MEMORIAM

13. The Review Committee is very saddened that one of its Members, Ms Sandra CHOW, Chairperson of Care for your Health - Cardiac Patients Mutual Support Association, passed away in late-December 2009 just before the completion of this review. Ms CHOW had participated actively in all meetings of the Review Committee as well as its subcommittees and had contributed many useful and constructive ideas from the patients' perspective on a wide range of topics. The Chairman and all Members of the Review Committee would like to express their deepest condolences to Ms CHOW's family.